REMARKS

Claim 11 has been amended to specify that the double stranded RNA is an isolated RNA to note that the RNA is free of other materials. Support for the amendment is found on page 19, lines 18-22. Claims 23-28 and 31-34 have been added to claim further embodiments of the invention. Support for new claims 23-28 and 31-34 is found throughout the specification including in original claims 5-9 and page 28, lines 12-31. New claim 29 is directed to another embodiment of the invention emphasizing the role of double stranded RNA as an adjuvant. Support for new claim 29 is found throughout the specification, including for example on page 1, lines 5-8, page 7 lines 24-30, page 19, lines 18-19 and page 22, line 32 through page 23, line 1. Claim 30 is added to claim a further embodiment of the present invention, specifying the interval between multiple rounds of administration. Support for new claim 30 is found through out the specification including for example on page 29, line 32 through line 2 of page 30.

Claims 11-14 stand rejected under 35 USC 103 as being unpatentable over Moldoveanu et al, in view of Wong et al. More particularly, the Examiner cites Moldoveanu for teaching a method of preventing an influenza infection by administering influenza HA protein and CpG DNA in an aqueous solution to the nasal musosa of mice. The Examiner then asserts that one of ordinary skill would have been motivated to modify the method of Moldoveanu to substitute the CpG DNA, taught by Moldoveanu with Poly (I:C). Applicants respectfully traverse this rejection.

First of all, applicants note that one of ordinary skill in the art would not have been motivated to combine teachings of the Wong et al (related to RNA) and Moldoveanu et al (related to DNA). It is well-known to the skilled artisan that the TLR receptor and signaling pathway for dsRNA are entirely different from those for CpG DNA, as shown in Exhibit A and Exhibit B. Thus double stranded RNA and CpG DNA were known to stimulate entirely different cell pathways. Accordingly, those skilled in the art would not have a reasonable expectation that one could substitute double stranded RNA for CpG DNA in the method of Moldoveanu et al to obtain similar predictable results. Furthermore, the secondary reference fails to provide any teaching regarding the administration of poly(I:C) and fails to teach or suggest that poly(I:C) could be used in combination with influenza antigens to induce a protective effect.

Applicants note that a careful reading of Wong et al reveals that Wong et al discloses the nasal or intraperitoneal administration of a poly(IC•LC) complex, not simply poly(IC). The poly(IC•LC)

complex is substantially different in structure relative to the isolated double stranded RNA (e.g.,poly(IC)) used in applicants' claimed invention. In particular, the poly(IC•LC) complex disclosed in Wong et al includes a poly-L-lysine carboxymethyl cellulose (LC) component (see page 2574, left column, lines 1-3 of Wong). Thus the complex used by Wong et al includes peptide bonds and glucoside bonds as well as double-stranded RNA.

Furthermore, the Wong teaching is further removed from applicant's claimed invention in that Wong fails to teach or suggest their complex could be used in combination with influenza antigens to enhance the immunological response to such antigens. In other words, Wong et al fails to disclose any adjuvant activity associated with the poly(IC•LC) complex. Wong et al simply teach that the administration of poly(IC•LC) alone provides a prophylactic effect against respiratory influenza A virus infection in mice. Accordingly, there is no teaching or suggestion in Wong et al to administer poly(IC•LC) in combination with microbes such as influenza antigens, and thus no motivation is provided that would lead one to combine the teachings of Wong with Moldoveanu.

Furthermore, applicants respectfully submit that the Examiner is overstating the teachings of Wong by stating "Wong teaches that Poly(I:C) provides a highly effective prophylaxis against respiratory influenza A infection in mice". Wong only conducted experiments using a complex of poly(I:C) and poly-L-lysine carboxymethyl cellulose. They provide no teaching as to the effects of Poly(I:C) itself. Specifically, the cited art is devoid of any suggestion that poly(IC•LC) complexes are equivalent to poly(IC) such that one skilled in the art would be motivated to substitute one for the other.

Applicants were the first to discover that an isolated double-stranded RNA (e.g., poly (I:C)) has efficacy as an adjuvant when combined with an influenza virus antigen(s). Additionally, not only does such a novel combination have non-virus-specific, interferon- or NK cell-mediated effects, but it also has virus-specific effects that have cross-protective activities between virus subtypes, i.e., effects on IgA increase for the prevention of mucosal infection and serum IgG increase for systemic immunoprotection (page 8, line 28 to page 9, line 2; page 36, lines 29-31; page 38, lines 9-28 of the present specification). Because Wong et al is directed to the use of a different entity (a poly-L-lysine carboxymethyl cellulose complex), and furthermore , even fails to suggest a composition comprising a combination of their complex with antigens, the reference simply fails to teach or suggest applicants novel combination and use.

Therefore, the skilled artisan would not have been motivated to combine teachings of above references, and the results would not have been predictable. Accordingly applicants respectfully submit

the Examiner has failed to establish a prima facie case of obviousness based on the teachings of the cited prior art references. The cited prior art for all its teachings fails to teach or suggest that double stranded RNA can be used as an adjuvant to enhance an immune response to influenza antigens.

Accordingly, applicants respectfully submit the cited references fail to teach or suggest applicants' use of the unique compositions as claimed in the amended claim set. Therefore, applicants respectfully request the withdrawal of the rejection of claims 11-14 under 35 USC 103 as being unpatentable over Moldoveanu et al, in view of Wong et al.

Applicants respectfully request allowance of the claims, and passage of the application to issuance. If any further discussion of this matter would speed prosecution of this application, the Examiner is invited to call the undersigned at (434) 220-2866.

Respectfully submitted,

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